Children's Health Protection Advisory Committee

December 20, 2011

Lisa P. Jackson, Administrator
United States Environmental Protection Agency
1200 Pennsylvania Ave, NW
Washington, DC 20460

RE: ORD Research Strategies Supporting Sustainability

Dear Administrator Jackson:

The Children's Health Protection Advisory Committee (CHPAC) has been following the planning that the US Environmental Protection Agency (EPA) Office of Research and Development (ORD) has undertaken to restructure thirteen ORD research programs into six major program areas. This letter summarizes CHPAC comments and questions concerning the new research framework and includes specific requests for more information from ORD staff in the coming year.

ORD personnel presented new ORD research strategies to the CHPAC on July 20, 2011. At the July meeting, CHPAC learned that ORD is incorporating the theme of sustainability into new research strategies and research plans for these new program areas. CHPAC members reviewed the strategies that ORD has publically shared[1]. In addition, at the November 16, 2011, CHPAC meeting, members heard a presentation on the 2011 National Academy of Sciences report "Sustainability and the US EPA"[2] from Dr. Bernard Goldstein; and learned about another advisory committee's (EPA National Advisory Council for Environmental Policy and Technology) focus on sustainability.

CHPAC recognizes the importance of the new research strategies as they are intended to guide research and research funding decisions into the future. CHPAC was pleased to hear from ORD staff that children's environmental health is one of two cross cutting, fundamental strategies of interest to ORD (the other being environmental justice).

It was clear from the July presentation that ORD does not intend to depart from the values encompassed in the 2000 ORD strategy report that described a program of children's environmental health research[3]. The 'take home' messages CHPAC heard from ORD echoed longstanding

[1] Request to EPA Science Advisory Board and EPA ORD Board of Scientific Counselors http://yosemite.epa.gov/sab/sabproduct.nsf/MeetingCal/794564E427071DFA8525780F00656E32?OpenDocument and ORD research frameworks

[2] National Research Council Committee on Incorporating Sustainability in the U.S. Environmental Protection Agency. (2011). *Sustainability and the U.S. EPA.* Washington, DC : National Academies Press. http://www.nap.edu/

[3] http://www.epa.gov/ncea/pdfs/strat4resrch.pdf

concerns expressed in CHPAC letters and recommendations to the agency. That is, that protection from environmental hazards early in life is fundamental to children's health and that health protection must be based on knowledge of the exposures and sensitivities that are unique to early life stages. The ORD spokesperson described many laudable ORD program achievements of which CHPAC has been very supportive. For example, CHPAC has advocated for the Children's Environmental Health Centers research program[4] and the National Children's Study as ways to develop the data and tools necessary to guide health protection.

The ORD presenter inferred that children's health protection will be fully incorporated into all of EPA's activities across each of the strategic goals of the Agency. With that in mind, interested CHPAC members spent time outside of the July meeting to examine the research strategy frameworks for Sustainable and Healthy Communities, Chemical Safety and Sustainability, and Human Health Risk Assessment in order to understand how children's environmental health (e.g., early life exposure research) would be addressed in the new strategies. The following comments are a reaction to how ORD has addressed children's environmental health in the new research strategies.

Overall:

CHPAC members note that there could not be any more powerful statement of sustainability than the recognition that what we do today must protect and nurture future generations. Sustainability can be defined by society's ability to preserve and improve the health and welfare of communities over generations. This definition applies to ecosystems and communities, and encompasses economic, societal, and environmental wellbeing. Protecting health during early life stages is fundamental to the concept of sustainability. Given that infants and children are often more sensitive and exposed to toxic substances than adults, a research focus on children's health is essential to EPA's emphasis on sustainability.

EPA's goal of sustainability is laudable and CHPAC is supportive of the new research strategy that is intended to integrate research areas that perhaps had previously been studied in isolation. CHPAC is also supportive of the seemingly convergent communication strategy of the ORD on the goal of reorganizing research around sustainability. Prior presentations to CHPAC have focused on individual ORD offices or individual media. The messages delivered at the July meeting were much more unified, coordinated, and cohesive. This trend of unification and coordination needs to be incorporated into all aspects of EPA communications and outreach. All of EPA should, as ORD has done, utilize the concepts of sustainability in EPA actions and communications.

CHPAC members noted that EPA has sponsored or developed excellent scientific research on children's environmental health in the past. However, findings from this research have not always been shared outside of a narrow scientific community. CHPAC members encourage EPA scientists and grantees to publish their work in scientific journals, government reports, and government newsletters[5]. ORD should develop outreach strategies to make research findings freely accessible to scientists, health care professionals, and community-based organizations, including school communities, with the understanding that each target audience requires different communication methods to assure that critical findings are shared in a timely manner.

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[4] http://yosemite.epa.gov/ochp/ochpweb.nsf/content/7252007.htm/$file/7252007.pdf
[5] For example, the EHS Bulletin (Environment, Health and Society research methods Bulletin) published by NCER (National Center for Environmental Research) http://www.epa.gov/ncer/ehs/ehsfall2011/ehs_bulletin_sept2011.pdf

Evaluation of the success of the new strategies will need to be clearly described. The metrics for sustainability are not obvious, and criteria for measuring the success of meeting the goals for sustainability are needed (perhaps in research plans that are developed from the research frameworks).

CHPAC would like to hear more from ORD on specific areas of the framework and strategies. Areas of special interest to CHPAC follow.

A. Chemical Safety for Sustainability

At the July meeting, an ORD spokesperson for the Chemical Safety for Sustainability Research Program (CSS) described program realignments that result in new research topic areas, such as inherency, systems modeling, and life cycle considerations. The CSS framework[6] contains much more detail on strategies for sustainability, and the CSS research action plan[7] provides information useful to CHPAC members interested in knowing how children's environmental health research will be advanced through the realignment.

By focusing on the populations and life stages most susceptible to harm, the health of the general population may be protected and promoted. This may mean putting a high priority on determining, for any particular chemical, whether hazards to early life stages have been appropriately and adequately evaluated. While great strides have been made over the past twenty years to ensure that life stage appropriate studies are conducted, most toxicological studies that are being used to develop regulatory standards and assess chemical safety were conducted using mature animals. While theses historical data are valuable, new studies must be designed to assess potential effects on prenatal and early life stages.

High throughput testing, which has been promoted as a method to rapidly build a new data base related to inherent chemical properties and cellular and molecular changes in response to a chemical, falls within the scope of the CSS research action plan. This new method of toxicity testing is expected to generate a large amount of data on early cellular and molecular changes that are predictive of adverse effects on human health and development. Several CHPAC members have expressed concerns that the potential for *in vitro* testing to predict chemical effects on embryogenesis, neurodevelopment, endocrine and immune function during early childhood is poorly understood at this time.

Members present at the July meeting raised the following points related to this research strategy:

1. ToxCast seems to be intended as a predictive model as opposed to being part of a tiered system of testing. There is a concern that if ToxCast rules out chemicals for further testing, biological effects relevant to early life stages could be missed.
2. Assurance that adverse effects relevant to early life are captured by testing systems such as ToxCast (or at least not dismissed) is needed. This was expressed as a need to validate the high throughput testing related to biological endpoints relevant to prenatal development and children's health.

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[6] http://yosemite.epa.gov/sab/sabproduct.nsf/7807842B9AD880F7852578B00040D27E/$File/CSS+Framework+1+June+2011.pdf

[7] http://yosemite.epa.gov/sab/sabproduct.nsf/23A995E7EDE63D26852578B20009D90B/$File/CSS+Draft+Research+Action+Plan+v1.pdf

3. The similarities between high throughput screening for toxicity and testing that result in screening out pharmaceutical chemicals was described. However, there is a fundamental difference in the result of a pharmaceutical company's rejection of a chemical for further development and developing a full understanding of what is "safe" for human exposure. Many, many tiers of additional pharmaceutical testing and use trials are necessary to demonstrate both efficacy and a lack of toxicity, while the current vision for Tox21 is additional tiers of testing to demonstrate toxicity rather than safety.
4. Some CHPAC members expressed concern that ToxCast is reductionist. While the conceptual approach for mixtures and multiple chemicals is understandable and laudable, there is a basic concern that focusing on what might be relatively few changes in protein expression or genomic change may not capture the potential range of interactions in the human body.
5. EPA seems to have assumed the burden of proof of sustainability and safety in the CSS research strategy. The contribution of industry is not apparent.

CHPAC members received an acknowledgement from ORD that EPA sees the issue of capturing and validating early life endpoints in high throughput testing as a concern. ORD described the new high-throughput assays as one guide to decision-making and explained that the current focus is on developing priorities for further testing. CHPAC members are pleased that Office of Children's Health Protection (OCHP) staff are providing input to EPA programs conducting computational toxicology work (for example, the virtual embryo project[8]) so that early life stages and developmental windows of vulnerability are comprehensively considered in the research.

CHPAC would like to hear more explicitly what health effects related to early life stage exposure and development (including prenatal and preconception exposure and development) will be incorporated into high throughput screening (e.g., assay selection for neurodevelopmental toxicity) and if specific health endpoint correlates are not included, what additional testing would be required before screening out a chemical for further research.

ORD suggested that with the possibility of conducting 8,000 simultaneous assays EPA anticipates a more comprehensive understanding of mixtures will emerge. CHPAC would like to hear explicitly how a systematic study of the cumulative effect of mixtures will be conducted in ways that can be correlated with whole animal studies. In addition, CHPAC would like to hear about both plans and outcomes for incorporating metabolic activation into high throughput research.

ORD is working on validation for testing that considers correlations, confounders, and dependent and independent variables for specific types of studies and assays. CHPAC will be a much more enthusiastic advocate of ToxCast and Tox21 testing once the potential for the new testing strategies to predict effects on growth, development, and function have been proven. CHPAC would like to see validation studies such as the recently published EPA computational toxicity research project on prenatal developmental toxicity[9]. CHPAC would like to hear more about plans for validating the relationship between *in vitro* and *in vivo* toxicity endpoints and see the results of this validation work.

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[8] http://www.epa.gov/ncct/v-Embryo/ focuses on early eye, vascular and limb developments and conducts experiments using stem cells and zebrafish to generate data

[9] Sipes, N.S. et al., 2011. Predictive Models of Prenatal Developmental Toxicity from ToxCast High-Throughput Screening Data. Toxicological Sciences 124(1), 109–127

CHPAC is concerned about translating this research, specifically in 1) explaining the complexity of this work to scientists, medical professionals, and community members; and 2) using this work to protect children by developing appropriate interventions based on this work and measuring the success of such interventions. CHPAC would like to hear ORD plans for sharing and using the results of the CSS work.

B. Sustainable and Healthy Communities

An ORD spokesperson discussed how the Sustainable and Healthy Communities Research Program (SHC) integrates multiple programs throughout ORD to work toward sustainable and healthy communities. This new strategy comprises aspects of the human health research program, land program (Superfund), and the ecosystems services program. Major SHC themes that relate to children's health research are related to tools and data collection, partner needs, and communities (such as children's settings and built environment factors). ORD described the SHC Children's Health Project, which has three tasks: 1) children's exposure factors (including a study of determinants of exposure to chemicals in the environment for early life stages); 2) health effects from early life exposures (and the latent or chronic effects resulting from early life exposures); and 3) systems approach to community-based children's health[10].

Members at the July meeting and subsequent discussions raised the following points related to this research strategy:

1. CHPAC members suggest that the social determinants of health model is a useful way to address multiple critical factors (such as economic disparities and environmental justice).
2. CHPAC did not hear a strong theme of addressing or acknowledging issues surrounding environmental justice.
3. CHPAC expressed concern that EPA may not have sufficient staff with the appropriate training and expertise (such as social scientists) for working with communities and their needs.
4. Members encouraged EPA to partner with groups that focus on learning environments across the childhood and adolescence trajectory, including child care and schools, and suggested that EPA determine the types of community capacity building that are successful and build on that knowledgebase.
5. It was not clear to members that EPA consistently includes preconception and prenatal lifestages in strategies aimed at children's health.
6. Members commented that it is important for EPA to sustain capacity building programs and that EPA should identify resources to sustain community efforts to improve environmental health.
7. CHPAC members noted that it is important to ensure that the community groups asked to participate in research programs and projects are actually part of the community, and suggested that existing community organizations provide excellent communication linkages to the community.
8. Members also suggest that Children's Environmental Health Centers integrate community participatory research methodology into all research and involve more

[10] Systems approach to community-based children's health: A research construct that interactions of factors, stressors, and exposures may result in children's health disparities; with the result that interventions may need to be just as complex and rooted in community environments.

representatives from the residents of the community they serve in their decision-making around research.

9. Members expressed some reservations about the concept of empowering communities to conduct risk assessments, as experience has shown that communities do not have the resources or expertise to conduct risk assessments, but expect state and federal agencies to provide guidelines and regulations that will ensure the public's safety.

CHPAC is interested in how social determinants of health can be explicitly, and in a measured way, incorporated into a systems approach to community-based children's health. CHPAC is interested in EPA's plans to transfer or translate the science to community action. A concern was expressed about the extent to which community and school based interventions have been proven effective (i.e., are proposed interventions grounded in science?).

Measures of success are needed in order to determine whether SHC work results in healthier and safer communities. CHPAC would like to hear ORD plans for measuring the progress of the SHC work.

C. Human Health Risk Assessment

Human Health Risk Assessment (HHRA) topics described in the ORD power point presentation included themes of dose response assessments (the Integrated Risk Information System); Integrated Science Assessments for criteria air pollutants; community and technical support for exposure and health assessments; and methods, models, and approaches to modernize risk assessment for the 21st century.

Members raised the following questions and points related to this research strategy:

1. What are the major research goals, timelines, and outcome measures? What childhood illnesses and developmental problems are being targeted and how are those associated with environmental exposures? What exposures are targeted and what is known about how those affect children's health? How will EPA measure its success or failure? Has past research been successful in reducing illness rates? How do current asthma rates compare with rates 10 and 20 years ago? Blood lead levels are lower, but attention deficit disorders and other learning problems seem to be more common and college entrance test scores are lower. Can the new research program explain these contradictory trends?
2. Environmental health research is most likely to produce a useful outcome when it targets a specific problem. CHPAC would prefer that EPA focus on improving children's health by identifying and reducing exposure to harmful substances instead of studying the effects of unabated exposures that are known or suspected to be hazardous.
3. CHPAC members have asked if additional children's exposure factors and risk information should be developed. There is concern among CHPAC that allergens and asthma triggers have not been assessed as rigorously as the approach used for chemicals. The Integrated Risk Information System is used for chemicals, not biologicals or pathogens, and work should be conducted to characterize risks from cockroach antigens, molds, harmful algae, and complex mixtures.
4. The EPA-funded Near Roadways Exposure to Urban Air Pollutants Study (NEXUS), a project of the University of Michigan, demonstrates that near roadway air pollution is a very important metric for exposures to urban pollutants. The relationship between the stage of pregnancy and level of exposure to pollutants is an important aspect of such research.

Questions were raised, as with other research areas, about measuring the result of HHRA utilizing a new research strategy. It was noted that approaches to human health risk assessment will continue to be used (that is, be sustainable) only if found useful. The question was asked how EPA will know that the result of the new strategy is improvements in children's health.

In addition to the three research strategies described above, CHPAC members discussed issues related to Safe and Sustainable Water Resources. Current requirements for tests done on drinking water and air are limited to a relatively small number of chemicals. When an unregulated contaminant is found in a drinking water supply at a level that exceeds EPA's one-day child health advisory, no action is required to be taken under the Safe Drinking Water Act. A question was raised about whether the Safe and Sustainable Water Resources Research Program will study children's exposure to unregulated contaminants of public drinking water, and if so, members asked what contaminants will be assessed, how many children are exposed, and what is the potential for an adverse health effect?

D. Research partners

In addition to discussing the individual strategies, CHPAC members expressed interest in the theme of overlapping research communities. Members encouraged EPA to partner with other agencies on research.

1. CHPAC members wondered if the CSS research will be limited to currently regulated chemicals and products. An emerging issue of interest to some members is the growing use of nanosilver and other nanomaterials. CHPAC is interested in knowing how EPA will work with other agencies to ensure the safety of these materials. Another group of chemicals of interest are pesticide residues in foods, water, and the indoor environment, which also may require collaboration with offices outside of ORD.
2. It was noted that more research is needed on endocrine disruption, childhood obesity, Type I and Type II diabetes, and developmental disorders including attention deficit and hyperactivity disorders. EPA and Centers for Disease Control and Prevention (CDC) could partner to identify the most prevalent childhood illnesses/disorders that seem to have an environmental component and work together to study causes and design interventions. CDC's Environmental Health Tracking Program and the National Institutes of Health (NIH)/EPA funded Children's Health Study have shared goals of reducing childhood illness and infant mortality and could work closely together.
3. CHPAC encourages ORD to compare research priorities among federal agencies (NIH, CDC, Department of Defense, Department of Education) and identify potential overlapping research and areas for collaboration.

In summary, CHPAC supports EPA's goal of sustainability and the integration and reorganization of research around this goal. The research frameworks provide a starting point for detailed research strategies, programs, and evaluation to achieve goals that include protecting children from environmental hazards.

CHPAC has many questions related to how implementation of the new research strategies will further our understanding of children's environmental health. The most pressing questions that CHPAC would like to discuss further with ORD are:

1. How social determinants of health can be explicitly and quantitatively incorporated into children's environmental health research;

2. How health effects related to early life stage (including preconception and prenatal periods) exposure and development will be addressed/incorporated into high throughput screening; and
3. How the research that results from the new research strategies and ORD reorganization be implemented into intervention strategies and evaluated (i.e., what metrics should be used) to assess whether children's environmental health has improved as a result of ORD's new research direction.

CHPAC will work with the Office of Children's Health Protection to request additional information and updates on ORD research plans.

Thank you for your consideration of our interest in continuing to discuss with ORD how sustainability and children's environmental health will be incorporated into the research of the newly organized ORD program areas.

Sincerely,

/Signed/

Pamela Shubat, Ph.D.
Chair
Children's Health Protection Advisory Committee

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